Table1
Agreement, sensitivity and specificity between the MRI definitions and K&L

	K&L≥1			K&L≥2		
	Agreement (%)	Sensitivity (%)	Specificity (%)	Agreement (%)	Sensitivity (%)	Specificity (%)
MRI TF OA	81.0	24.0	94.5	91.6	55.8	93.1
MRI PF OA	79.2	15.9	94.3	89.9	22.4	93.0
MRI TF and/or PF OA	79.3	31.5	90.6	87.3	59.7	88.5

K&L: Kellgren and Lawrence classification system; MRI: Magnetic resonance Imaging; PF OA: patellofemoral osteoarthritis; TF OA: tibiofemoral osteoarthritis. K&L is reference standard.

No significant associations were found for prediction of new knee pain after 2 years.

Conclusions: In this early OA population, the agreement of the MRI definition for knee OA and the reference standard K&L criteria is good. Compared to the K&L criteria there were twice as many cases 'diagnosed' with knee OA using the MRI definition (TF OA). The association of the MRI definition and knee pain is similar to the association between the K&L criteria and knee pain. The lack of association between PF OA and most knee pain definitions might be due to a lack of other features, such as bone marrow lesion, in the MRI definition. None of the definitions predicts new knee pain at 2 years follow-up.

345
BONE MARROW LESION REGRESSION IS ASSOCIATED WITH WORSENING PERI-ARTICULAR BONE: DATA FROM THE OSTEOARTHRITIS INITIATIVE

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Purpose: Reducing bone marrow lesion (BML) size (BML regression) may represent an important therapeutic goal for modifying osteoarthritis (OA) progression. However, the relationship between the progression and regression of BMLs and knee OA progression remains poorly understood. We evaluated the associations between BML volume change and changes in peri-articular bone mineral density (paBMD), a measure of bone quality, as well as radiographic scoring of subchondral sclerosis to better understand the role of bone remodeling in these relationships.

Methods: The sample comprised 404 participants in the Osteoarthritis Initiative (OAI) with weight-bearing posterior-anterior knee radiographs and magnetic resonance images (MRI) at the 24- and 48-month visits as well as dual-energy x-ray absorptiometry (DXA) at the 30-/36-month and 48-month visits. The right knee was assessed unless contraindicated. We used knee DXA scans to derive medial tibia (MT) paBMD and a paBMD ratio (MT paBMD divided by lateral tibia (LT) paBMD [M:L paBMD]; ICC > 0.99). Knee radiographs were scored for sclerosis (grades 0 to 3) in the MT (test-retest kappa = 0.76). Two raters determined BML volume on sagittal fat-suppressed MRI using a semi-automated segmentation method (ICC = 0.59 - 0.93). BML volume was calculated for the MT and LT. We excluded knees with LT BML volumes $\geq 0.50\ cm^3$ (at 24- or 48-month OAI visits) because we wanted to ensure that the LT was a good reference region for the M:L paBMD ratio, particularly since we were interested in changes in the MT. The cut point for LT BMLs was based on preliminary univariate analyses that suggested moderate-large BMLs were associated with M:L paBMD and M:L paBMD change. The MT BML volume change was classified into quartiles. We chose the middle two quartiles of BML volume change as the reference group. We used logistic regression models to evaluate the association between quartiles of changes in MT paBMD or M:L paBMD ratio, as outcomes, and change in MT BML volume (classified into three groups). The models were adjusted for age (<65 years, ≥ 65 years) and obesity (body mass index < 30 kg/m^2, ≥ 30 kg/m^2). Since only a small number of knees increased MT sclerosis scores we used Fisher Exact Tests to explore if the frequency of knees with sclerosis progression was different between BML volume change groups.

Results: The sample (n = 310), excluding those with LT BMLs, is described in the table. We found an association between greater MT paBMD change and BML regression (OR = 1.7 [95% CI = 1.1 - 2.8]) and a similar trend for BML progression (OR = 1.6 [95% CI = 1.0 - 2.6]). We also detected an association between increased M:L paBMD change and BML regression (OR = 1.6 [95% CI = 1.0 - 2.7]) or BML progression (OR = 1.8 [95% CI = 1.1 - 3.0]), although BML regression had borderline statistical significance. Exploratory analyses indicated that the frequency of sclerosis progression in the MT was greater among knees with BML progression or regression compared to knees with no BML change (p = 0.01 and p = 0.04; respectively).

Conclusions: Based on increased paBMD and sclerosis progression in the MT, knees with BML regression or BML progression were more likely to have peri-articular bone changes related to OA progression compared to knees with no BML change. BML regression on traditional MRI may not reflect an improvement in peri-articular bone quality.

346
THE RELATION BETWEEN QUANTITATIVE DELAYED CONTRAST-ENHANCEMENT IN MENISCUS AND CARTILAGE IN KNEE OSTEOARTHRITIS

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Purpose: Quantitative analysis of delayed contrast-enhanced T1 values (T1GD) was proposed to give insight in meniscal damage and articular cartilage degeneration within one MR examination. However, unlike in delayed gadolinium-enhanced MRI of cartilage (dGEMRIC), contrast uptake in the meniscus is probably not determined by the glycosaminoglycan (sGAG) content and hence fixed charged density in the meniscus, but is rather based on the integrity of the collagen network. Despite the different factors which are believed to dominate contrast uptake in the meniscus and cartilage, it has been shown that there is a moderate relation of T1GD values of the meniscus and the adjacent cartilage in healthy volunteers and self-reported knee OA patients. This relation has, however, not yet been studied in patients diagnosed with OA. Therefore, the goal of this study was to explore the relation between

Table
Descriptive Characteristics of Knees with Medial Tibia Bone Marrow Lesion (BML) Regression, Progression, or No Change

Variable	BML Regression (n = 77) Median (Min, Max) or n (%)	No BML or No BML Change (n = 156) Median (Min, Max) or n (%)	BML Progression (n = 77) Median (Min, Max) or n (%)
Age (years)	65 (50, 81)	61 (48, 82)	68 (48, 82)
Body mass index (kg/m^2)	29.3 (21.1, 40.9)	29.4 (20.1, 42.0)	29.5 (19.6, 40.7)
Female	40 (52.0%)	85 (54.5%)	39 (50.7%)
Kellgren-Lawrence Grade ≥2	62 (80.5%)	95 (61.3%)	57 (74.0%)
BML Volume Change (cm^3)	-0.37 (-8.44, -0.14)	-0.02 (-0.13, 0.03)	0.21 (0.04, 6.77)
Medial Tibia paBMD (Change)	0.002 (-0.149, 0.164)	-0.011 (-0.107, 0.149)	-0.001 (-0.091, 0.168)
M:L paBMD Ratio (Change)	0.005 (-0.119, 0.291)	-0.007 (-0.102, 0.091)	0.003 (-0.080, 0.410)
Sclerosis Progression (Medial Tibia)	5 (6.9%)	2 (1.3%)	7 (10%)

Notes: paBMD: peri-articular bone mineral density, M:L paBMD Ratio: medial-to-lateral paBMD ratio.

T1GD values of the meniscus and the adjacent articular cartilage in knee OA patients. This may give insight in the different factors which dominate contrast uptake in the meniscus and cartilage in an OA knee.
Methods: We analyzed data of 17 knee OA patients (KL grade I and II) previously used to investigate the reproducibility of dGEMRIC. All examinations were performed on a 3 Tesla MRI scanner using a custom made open design 3-channel knee coil, enabling imaging of large diameter OA knees. T1GD relaxation times in the anterior (antM) and posterior horn (postM) of the meniscus and in the adjacent weight-bearing femoral (wbFC) and tibial (wbTP) cartilage in the medial and lateral tibiofemoral compartment were calculated in manually drawn regions of interest. T1GD values in all regions (meniscus and cartilage) in the medial and lateral compartment were compared using the Mann-Whitney test. In addition, the correlation coefficients between T1GD values of the meniscus and cartilage were calculated to assess the relation between degeneration of both structures.
Results: Median meniscus and cartilage T1GD values in the medial and lateral tibiofemoral joint are listed in Table 1. The correlation between T1GD values in the meniscus and adjacent cartilage regions was moderate in the lateral and strong in the medial tibiofemoral compartment (Table 2). An example of a meniscus and adjacent cartilage with relatively low T1GD values and a meniscus with adjacent cartilage with relatively high T1GD values is shown in Figure 1.

Table I
Median $T1_{GD}$ values with 25^{th} - 75^{th} percentile

Region	Lateral compartment	Medial compartment	P
antMT1$_{GD}$ (ms)	413 (375 -435)	350 (315-485)	ns
postM T1$_{GD}$(ms)	404 (330-441)	382 (314-355)	ns
wbFC T1$_{GD}$ (ms)	510 (466-574)	433 (410-506)	0.04
wbTP T1$_{gd}$ (ms)	607 (463 - 664)	465 (430 - 566)	0.04

Table 2
Correlation between $T1_{GD}$ of meniscus and adjacent cartilage with 95% CI.

Lateral compartment	wbFC	wbTP
antM	R = 0.78 95% CI = 0.48-0.92	R = 0.75 95% CI = 0.42 - 0.90
postM	R = 0.73 95% CI = 0.38-0.89	R = 0.73 95% CI = 0.38 - 0.90
Medial compartment	wbFC	wbTP
anIM	R = 0.95 95% CI = 0.86-0.98	R = 0.88 95% CI = 0.68 - 0.95
postM	R = 0.88 95% CI = 0.69-0.96	R = 0.83 95% CI = 0.57 - 0.94

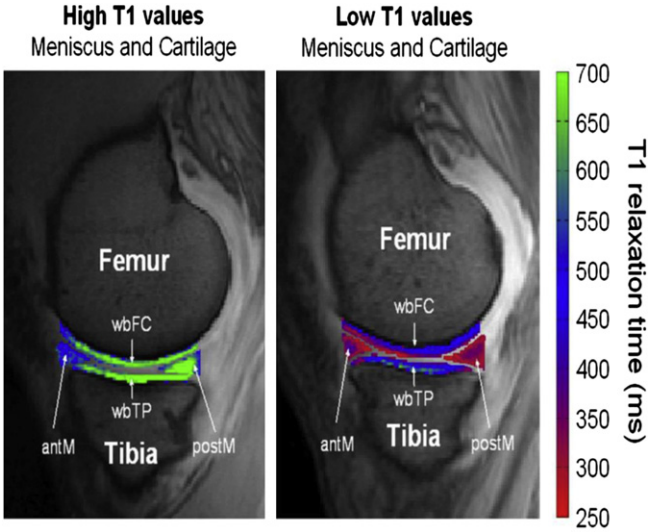

Figure 1. Example of m eniscus with adjacent cartilage with relatively high and low $T1_{GD}$.

Conclusions: The results of the present study show a strong correlation between meniscus and cartilage T1 values after intravenous injection of an ionic contrast agent. This observation suggests a similar degree of degeneration of meniscus and cartilage in OA, which is in agreement with previous research using conventional MRI scores as measure for degeneration. However, the strong relation between ionic contrast uptake in the meniscus and cartilage together with the knowledge that contrast uptake in the meniscus is mainly based on collagen network integrity and not on the fixed charge density, suggests that dGEMRIC may not be as sGAG specific as thought before. Cartilage collagen integrity and/or orientation may also influence ionic contrast uptake in OA cartilage. This hypothesis is being supported by recent work of other groups. Therefore, dGEMRIC T1GD outcomes in knee OA must be interpreted with caution in future investigations.

347
SCHEUERMANN'S DISEASE: EVALUATION OF RADIOLOGICAL CRITERIA AND POPULATION PREVALENCE

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Purpose: Scheuermann's disease is a form of osteochondrosis of the spine, characterized by increased posterior rounding of the thoracic spine with structural deformity of the vertebral elements. Different expert-opinion based radiological criteria have been suggested for diagnosing Scheuermann's disease, yet these have not been validated. The prevalence of Scheuermann's disease in the general population reported ranges from 1% to 10%. Our aim was to determine the prevalence of Scheuermann's disease in a Dutch population and evaluate the consistency of radiographic diagnostic criteria.
Methods: The youngest cohort of the population-based Rotterdam Study (RS-III) including 2,753 participants aged 45-89 years was radiologically assessed for Scheuermann's disease criteria. Vertebral body endplate irregularities, vertebral wedging, and thoracic kyphosis angle were evaluated on thoracolumbar lateral spine radiographs. The radiographic criteria of Sørensen and Sachs et al. were applied in two phases to diagnose Scheuermann's disease. In the first phase, we distinguished potential cases from normal radiographs based on vertebral wedging at a minimum of three vertebral levels and presence of vertebral body endplate irregularities. Cohen's kappa statistics were calculated for inter-rater agreement of these individual criteria. Next, we re-evaluated these potential cases by measuring the thoracic kyphosis angle to diagnose Scheuermann's disease and the disease prevalence was estimated. Additionally, we evaluated the impact of varying the kyphosis angle criterion on prevalence estimation of Scheuermann's disease. Sex-combined and gender-specific prevalence estimates were calculated and gender differences were tested with Pearson's chi-square test.
Results: Of the 2,753 participants, 677 individuals (24.6%) had endplate irregularities and 140 (5.1%) had vertebral wedging. Of these, 127 had both criteria. These abnormalities were significantly more prevalent among men ($p<0.05$). The inter-rater agreement was substantial with kappa statistics of 78.8% for vertebral wedging and 79.4% for endplate irregularity. In addition, 111 of those fulfilling both diagnostic criteria had a kyphosis angle greater than 45 degrees, resulting in a prevalence estimate of 4.0% (95% CI:3.3%-4.7%) of Scheuermann's disease. The disease prevalence was 4.5% in men vs. 3.6% in women, yet this difference was not statistically significant ($p=0.23$). In addition, we evaluated the impact of varying diagnostic criteria on prevalence estimation of Scheuermann's disease. By adjusting the kyphosis angle criterion from 45 degrees to 40 or 35 degrees, we found that this would increase the total number of Scheuermann's disease cases marginally (115 and 121, resp 4.4% [3.6%-5.2%], respectively) for the total population.
Conclusions: Our results revealed a prevalence estimate of 4.0% of Scheuermann's disease in Dutch individuals aged 45 years and over. Even though there is no current gold standard for the radiographic definition, standardized scoring of independent features resulted in substantial inter-observer agreement, and different applications of diagnostic criteria did not significantly alter disease classification.

348
EARLY CARTILAGE INJURY QUANTIFIED AND CHARACTERIZED WITH MULTIPHOTON MICROSCOPY IMAGING

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